

Claims

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1. Method to determine the presence or the absence of at least one target nucleic acid by reference to at least one control nucleic acid, which comprises processing said target nucleic acid so as to allow its detection, submitting said control nucleic acid to comparable processing conditions, and validating or invalidating the detection result obtained for said target nucleic acid by comparing it to the detection result obtained for said control nucleic acid,

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wherein said control nucleic acid is provided by a solid support onto which it is adsorbed, and from which a definite amount thereof is to be desorbed, whereby there is provided an essentially quantitatively reproducible and controlled amount of said control nucleic acid for submission to said comparable processing conditions.

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2. Method according to claim 1,
said method comprising the steps of:

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- providing with said solid support comprising said at least one control nucleic acid adsorbed thereon, and contacting said solid support with a liquid medium, so as to allow a definite amount of said control nucleic acid to be desorbed from said solid support into said liquid medium, substantially without affecting the primary sequence of said control nucleic acid;

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- optionally, further processing the resulting liquid medium containing said control nucleic acid;
 - submitting said control nucleic acid which is contained in or originating from said resulting, optionally further processed, liquid medium, to comparable processing conditions, so that it constitutes a processing control by reference to the processing of said target nucleic acid;
 - determining whether said target nucleic acid is detected or not, and determining whether said control nucleic acid is detected or not;
 - comparing the target nucleic acid detection result to the one of said control nucleic acid, so as to validate or invalidate the target nucleic acid detection result;
- wherein said processing comprises at least one processing step selected from the group constituted by amplification, including PCR amplification, gel electrophoresis, Southern analysis, northern analysis, hybridization including probe-mediated hybridization, and combinations thereof.
3. Method according to any one of claims 1-2, wherein said solid support comprises at least one membrane.
 4. Method according to the preceding claim, wherein said membrane material is selected from the group constituted by cellulose, cellulose-derived materials including chemically-treated celluloses, glass fibers, nylons, polyethersulfones, polypropylene, woven porous polymers, non-woven porous polymers, PTFE, porous glasses, and PVDF.

5. Method according to any one of claims 3-4, wherein said membrane material is selected from the group constituted by cellulose, cellulose-derived materials including chemically-treated celluloses, glass fibers, nylons, polyethersulfones, and polypropylene; preferably from the group constituted by cellulose, cellulose-derived materials and nylons.
6. Method according to any one of claims 3-5, wherein said membrane has a thickness in the range 50-3000 microns, preferably 100-1500 microns, more preferably 150-1000 microns.
7. Method according to any one of claims 3-6, wherein said membrane has the shape of a disk, a square, a rectangle or a strip.
8. Method according to any one of claims 1-7, wherein said solid support further comprises at least one carrier agent adsorbed thereon.
9. Method according to the preceding claim, wherein said carrier agent is selected from the group constituted by:
- nucleic acids unrelated or heterologous to said control nucleic acid, so as to substantially not interfere in the detection processing of said control nucleic acid;
 - albumins.
10. Method according to any one of claims 8-9, wherein said carrier agent is a nucleic acid unrelated or heterologous to said control nucleic acid and also

unrelated or heterologous to said target nucleic acid, so as to substantially not interfere in the detection processing of said control and said target nucleic acids.

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11. Method according to any one of claims 8-10, wherein said carrier agent is selected from the group constituted by polyA, polyG, polyC, polyT, polydA, polydG, polydC, polydT, polydU, homopolydeoxyribonucleotides, homopolyribonucleotides, block-polymers of deoxyribonucleotides, block-polymers of ribonucleotides, block-polymers of deoxyribonucleotides and ribonucleotides, and mixtures thereof.

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12. Method according to any one of claims 8-10, wherein said carrier agent is selected from the group constituted by:

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- fish DNA, such as herring DNA, especially herring sperm DNA, and salmon DNA, especially salmon sperm DNA, and mixtures thereof;
- albumins, especially bovine serum albumin (BSA).

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13. Method according to any one of claims 8-11, wherein said carrier agent is selected from the group constituted by:

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- homopolydeoxyribonucleotides, block-polymers of deoxyribonucleotides, and mixtures thereof;
- albumins, especially bovine serum albumin (BSA).

14. Method according to any one of claims 1-13, wherein said control nucleic acid is selected from the group constituted by positive controls, negative

controls, internal controls, external controls, qualitative controls, semi-quantitative controls, quantitative controls, real-time amplification controls, and combinations thereof.

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15. Method according to any one of claims 1-14, wherein said nucleic acid processing for detection comprises at least one nucleic acid extraction and/or purification step, prior to said nucleic acid detection step.

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16. Method according to any one of claims 1-15, wherein said processing comprises a detection step involving at least one hybridization step.

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17. Method according to any one of claims 1-16, wherein said processing comprises a detection step involving at least one PCR or RT-PCR, especially real-time and quantitative PCR or RT-PCR.

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18. Method according to any one of claims 1-17, wherein said target nucleic acid detection is a quantitative detection, preferably a real-time quantitative detection.

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19. Method according to any one of claims 1-18, wherein said control nucleic acid detection is a quantitative detection, preferably a real-time quantitative detection.

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20. Solid support for at least one control nucleic acid, said solid support being specifically adapted for carrying out a method for the determination of presence or absence of at least one target nucleic

acid by reference to at least one control nucleic acid according to any one of claims 1-19, said solid support comprising:

- 5 - at least one absorbent support made of a material whose composition and structure allow for non covalent adsorption of said control nucleic acid onto said solid support, and which is or has been heat-treated and/or chemically-treated so as to be essentially devoid of any enzymatic activity;
- 10 - at least one carrier agent adsorbed thereon, which facilitates the adsorption of said control nucleic acid onto said solid support and/or facilitates the desorption of said control
- 15 nucleic acid from said solid support and/or promoting the stability of said control nucleic acid on said solid support, especially in the course of storage, substantially without affecting the primary sequence of said control
- 20 nucleic acid;
- optionally, said control nucleic acid adsorbed thereon;

wherein:

- 25 - said carrier agent is selected from the group of albumins; or
- said solid support comprises said control nucleic acid adsorbed thereon, and said carrier agent is selected from the group constituted by nucleic acids unrelated or heterologous to said
- 30 control nucleic acid and/or to said target nucleic acid, so as to generally not interfere in the detection method.

21. Solid support according to the preceding claim, wherein said carrier agent is a nucleic acid unrelated to any naturally occurring human nucleic acid.

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22. Solid support according any one of claims 20-21, wherein said carrier agent is a nucleic acid unrelated to any nucleic acid originating from nucleic acid originating from any naturally occurring agent being pathogen to a mammalian, especially to human.

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23. Solid support according to any one of claims 20-22, wherein said carrier agent is selected from the group constituted by:

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- polyA, polyG, polyC, polyT, polydA, polydG, polydC, polydT, polydU, homopolydeoxyribonucleotides, homopolyribonucleotides , block-polymers of deoxyribonucleotides, block-polymers of ribonucleotides, block-polymers of deoxyribonucleotides and ribonucleotides, and mixtures thereof;
- fish DNA;
- albumins.

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24. Solid support according to any one of claims 20-22, wherein said carrier agent is selected from the group constituted by:

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- homopolydeoxyribonucleotides such as polydA, block-polymers of deoxyribonucleotides, and mixtures thereof;

- herring DNA, especially herring sperm DNA, and salmon DNA, especially salmon sperm DNA, and mixtures thereof;
- albumins, such as bovine serum albumin (BSA).

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25. Solid support according to any one of claims 20-24, wherein said carrier agent is selected from the group constituted by:

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- homopolydeoxyribonucleotides such as polydA, block-polymers of deoxyribonucleotides, and mixtures thereof;
- albumins, such as bovine serum albumin (BSA).

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26. Solid support according to any one of claims 20-25, wherein said carrier agent comprises :

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- 0.1-50 μg of nucleic acids, preferably 1-10 μg , more preferably 4-8 μg , even more preferably 5-6 μg , or
- 2-100 μg of albumin (e.g. BSA), preferably 5-50 μg , more preferably 10-30 μg , even more preferably 15-20 μg .

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27. Solid support according to any one of claims 20-26, wherein said support comprises at least one membrane.

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28. Solid support according to the preceding claim, wherein said membrane material is selected from the group of cellulose, cellulose-derived materials including chemically-treated celluloses, glass fibers, nylons, polyethersulfones, polypropylene, woven porous polymers, non-woven porous polymers, PTFE, porous glasses, and PVDF.

29. Solid support according to any one of claims 27-28,
wherein said membrane material is selected from the
group constituted by cellulose, cellulose-derived
materials including chemically-treated celluloses,
glass fibers, nylons, polyethersulfones, and
polypropylene.
30. Solid support according to any one of claims 27-29,
wherein said membrane material is selected from the
group of cellulose, cellulose derived materials and
nylons.
31. Solid support according to any one of claims 27-30,
wherein said membrane has a thickness in the range
50-3000 microns, preferably 100-1500 microns, more
preferably 150-1000 microns.
32. Solid support according to any one of claims 27-31,
wherein said membrane has the shape of a disk, a
square, a rectangle or a strip.
33. Solid support according to any one of claims 27-32,
wherein said membrane has a surface in the range
10-500 mm², preferably 20-250 mm², more preferably
30-200 mm².
34. Solid support according to any one of claims 20-33,
wherein said enzymatic activity comprises nuclease
activity, including DNase and/or RNase activity.
35. Solid support according to any one of claims 20-34,
wherein said solid support further comprises at
least one control nucleic acid adsorbed thereon.

36. Solid support according to the preceding claim,
wherein said control nucleic acid is selected from
the group constituted by positive controls,
negative controls, internal controls, external
controls, qualitative controls, semi-quantitative
controls, quantitative controls, real-time
amplification controls, and combinations thereof.
37. Solid support according to any one of claims 35-36,
wherein said control nucleic acid is adsorbed in an
amount in the range 10 - 10^8 copies, preferably 10^2 -
 10^5 copies.
38. Solid support according to any one of claims 35-37,
wherein said control nucleic acid is adsorbed in an
amount in the range 10 - 1000 copies, preferably 20 -
 500 copies, more preferably 50 - 100 copies.
39. Series of supports which comprises a plurality of
supports according to any one of claims 35-38,
wherein each of said supports carries a different
standardized amount of the same control nucleic
acid adsorbed thereon, such that said series of
supports provides with a calibration range of said
control nucleic acid, preferably in the range 10 -
 10^8 copies, more preferably 10^2 - 10^5 copies, even
more preferably 20 - 500 copies, most preferably 50 -
 100 copies.
40. Process for the manufacture of a solid support
according to any one of claims 20-38, said process
comprising the steps of:
- providing with an absorbent support material;

- heat-treating and/or chemically-treating said support, so as to essentially remove any nuclease activity;
- depositing at least one carrier agent onto said support material; and,
- optionally, depositing at least one control nucleic acid onto said support material so as to adsorb the desired amount of said control nucleic acid onto said support.

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41. Process according to the preceding claim, wherein said heat treatment is performed at a temperature in the range from 100°C to 180°C.

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42. Process according to any one of claims 40-41, wherein said chemically treating comprises a DEPC (Diethyl-pyrocabonate) treatment.

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43. Process according to any one of claims 40-42, wherein said depositing step(s) comprise(s) at least one spotting step.

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44. Process according to any one of claims 40-43, wherein said depositing step(s) comprise(s) at least one drying step.

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45. Process according to the preceding claim, wherein said drying step is performed at a temperature in the range from 45°C to 70°C, preferably at around 60°C.

46. Kit comprising:

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- at least one solid support according to 20-38 and/or at least one series of solid supports according to claim 39;
 - optionally, a dispenser for distributing said solid support into a container; and,
 - instructions for the use thereof.

47. Kit according to the preceding claim, wherein said kit is selected from the group constituted by:
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- Kit for nucleic acid extraction and/or purification;
 - Kit for nucleic acid detection;
 - Kit for nucleic acid amplification, including PCR amplification, RT-PCR amplification, real-time PCR, quantitative PCR;
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 - Kit for the diagnosis of a disease or a condition.

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